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NEWS	7	MAY 19	Derwent World Patents Index to be reloaded and enhanced
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NEWS EXPRESS			JUNE 30 CURRENT WINDOWS VERSION IS V8.01b, CURRENT MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP), AND CURRENT DISCOVER FILE IS DATED 26 JUNE 2006.
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FILE 'HOME' ENTERED AT 09:56:43 ON 06 JUL 2006

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COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	0.21	0.21

FILE 'MEDLINE' ENTERED AT 09:57:14 ON 06 JUL 2006

FILE 'EMBASE' ENTERED AT 09:57:14 ON 06 JUL 2006

FILE 'BIOSIS' ENTERED AT 09:57:14 ON 06 JUL 2006

FILE 'SCISEARCH' ENTERED AT 09:57:14 ON 06 JUL 2006

FILE 'CAPLUS' ENTERED AT 09:57:14 ON 06 JUL 2006


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=> s complex
L1     4295595 COMPLEX

=> s l1 and hemostatic dysfunction
L2          17 L1 AND HEMOSTATIC DYSFUNCTION

=> s l2 and "c-reactive protein"
L3           5 L2 AND "C-REACTIVE PROTEIN"

=> s l3 and VLDL
L4           1 L3 AND VLDL

=> d l4 cbib abs
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L4 ANSWER 1 OF 1 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN
2002:541408 Document No.: PREV200200541408. Biphasic transmittance waveform in the APTT coagulation assay is due to the formation of a Ca++-dependent complex of C-reactive protein with very-low-density lipoprotein and is a novel marker of impending disseminated intravascular coagulation. Toh, Cheng Hock; Samis, John; Downey, Colin; Walker, John; Becker, Lev; Brufatto, Nicole; Tejidor, Liliana; Jones, Greg; Houdijk, Wim; Giles, Alan; Koschinsky, Marlys; Ticknor, Larry O.; Paton, Ray; Wenstone, Richard; Nesheim, Michael [Reprint author]. Department of Biochemistry, Queen's University, Botterell Hall, Room A210, Kingston, ON, K7L 3N6, Canada. nesheimm@post.queensu.ca. Blood, (October 1, 2002) Vol. 100, No. 7, pp. 2522-2529. print.
CODEN: BLOOAW. ISSN: 0006-4971. Language: English.

AB A decrease in light transmittance before clot formation, manifesting as a biphasic waveform (BPW) pattern in coagulation assays, was previously correlated with the onset of disseminated intravascular coagulation (DIC). In this study of 1187 consecutive admissions to the intensive care unit, the degree of this change on admission predicts DIC better than D-dimer measurements. Additionally, the BPW preceded the time of DIC diagnosis by 18 hours, on average, in 56% (203 of 362) of DIC patients. The BPW is due to the rapid formation of a precipitate and coincident turbidity change on recalcification of plasma. The isolated precipitate contains very-low-density lipoprotein (VLDL) and C-reactive protein (CRP). The addition of CRP and Ca++ to normal plasma also causes the precipitation of VLDL and IDL, but not LDL or HDL. The Kd of the CRP/VLDL interaction is 340 nM, and the IC50 for Ca++ is 5.0 mM. In 15 plasmas with the BPW, CRP was highly elevated (77-398 mug/mL), and the concentration of isolated VLDL ranged from 0.082 to 1.32 mM (cholesterol). The turbidity change on recalcification correlates well with the calculated level of the CRP-VLDL complex. Clinically, the BPW better predicts for DIC than either CRP or triglyceride alone. The complex may have pathophysiological implications because CRP can be detected in the VLDL fraction from sera of patients with the BPW, and the

VLDL fraction has enhanced prothrombinase surface activity. The complex has been designated lipoprotein complexed C-reactive protein.

=> dup remove l3
PROCESSING COMPLETED FOR L3
L5 5 DUP REMOVE L3 (0 DUPLICATES REMOVED)

=> d l5 1-5 cbib abs

L5 ANSWER 1 OF 5 CAPLUS COPYRIGHT 2006 ACS on STN
2006:538913 Document No. 145:23858 Method for diagnosing critically ill patients by measuring the formation of lipoprotein-C-reactive protein complex in the presence of a surfactant. Jones, Gregory Ray; Borzhemskaya, Larisa; Hanson, Donald G.; Estevez, Rafael Angel; Wilson, Mark S.; Link, John Glenn; Barnes, Bryan (Biomerieux, Inc., USA). PCT Int. Appl. WO 2006060386 A1 20060608, 37 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IS, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2005-US43120 20051130. PRIORITY: US 2004-632431P 20041201.

AB Provided is an improved method of diagnosing and monitoring hemostatic dysfunction, sepsis-related morbidity or severe infection by improving detection of an in vitro complex formed by lipoprotein and C-reactive protein with the utilization of an effective amount of a surface active agent in the reagent. The method includes: (a) obtaining a patient sample; (b) combining said sample with a reagent comprising a divalent cation and an effective amount of a surface active agent to form a reaction mixture; and (c) examining said reaction mixture to determine whether an LC-CRP complex is formed to diagnose or monitor patients having hemostatic dysfunction, sepsis-related morbidity or severe infection.

L5 ANSWER 2 OF 5 EMBASE COPYRIGHT (c) 2006 Elsevier B.V. All rights reserved on STN
2005440467 EMBASE A case of reversible posterior leukoencephalopathy syndrome caused by transient hypercoagulable state induced by infection. Yano Y.; Kario K.; Fukunaga T.; Ohshita T.; Himeji D.; Yano M.; Nakagawa S.; Sakata Y.; Shimada K.. Dr. Y. Yano, Department of Internal Medicine, Nango National Health Insurance Hospital, Ohaza Mikado 1078, Nango Village, Miyazaki 883-0306, Japan. yyano@jichi.jp. Hypertension Research Vol. 28, No. 7, pp. 619-623 2005.
Refs: 27.
ISSN: 0916-9636. CODEN: HRESE4
Pub. Country: Japan. Language: English. Summary Language: English.
Entered STN: 20051020. Last Updated on STN: 20051020

AB We report a normotensive case of reversible posterior leukoencephalopathy syndrome caused by transient hypercoagulable state. Hypertension is the main risk factor for reversible posterior leukoencephalopathy syndrome, which is believed to occur as a result of high blood pressure-related dysfunction of cerebrovascular endothelial cells, because it commonly appears in hypertensive emergency. However, in this completely normotensive case, the typical clinical findings of reversible posterior leukoencephalopathy syndrome were triggered by transient hypercoagulable state without any blood pressure variation. The case was successfully treated with anticoagulation therapy using heparin. Thus, this case indicates that reversible posterior leukoencephalopathy syndrome is induced by cerebrovascular endothelial dysfunction, which is induced not

only by high blood pressure but also hemostatic dysfunction.

L5 ANSWER 3 OF 5 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN
2002:541408 Document No.: PREV200200541408. Biphasic transmittance waveform in the APTT coagulation assay is due to the formation of a Ca++-dependent complex of C-reactive protein with very-low-density lipoprotein and is a novel marker of impending disseminated intravascular coagulation. Toh, Cheng Hock; Samis, John; Downey, Colin; Walker, John; Becker, Lev; Brufatto, Nicole; Tejidor, Liliana; Jones, Greg; Houdijk, Wim; Giles, Alan; Koschinsky, Marlys; Ticknor, Larry O.; Paton, Ray; Wenstone, Richard; Nesheim, Michael [Reprint author]. Department of Biochemistry, Queen's University, Botterell Hall, Room A210, Kingston, ON, K7L 3N6, Canada. nesheimm@post.queensu.ca. Blood, (October 1, 2002) Vol. 100, No. 7, pp. 2522-2529. print.
CODEN: BLOOAW. ISSN: 0006-4971. Language: English.

AB A decrease in light transmittance before clot formation, manifesting as a biphasic waveform (BPW) pattern in coagulation assays, was previously correlated with the onset of disseminated intravascular coagulation (DIC). In this study of 1187 consecutive admissions to the intensive care unit, the degree of this change on admission predicts DIC better than D-dimer measurements. Additionally, the BPW preceded the time of DIC diagnosis by 18 hours, on average, in 56% (203 of 362) of DIC patients. The BPW is due to the rapid formation of a precipitate and coincident turbidity change on recalcification of plasma. The isolated precipitate contains very-low-density lipoprotein (VLDL) and C-reactive protein (CRP). The addition of CRP and Ca++ to normal plasma also causes the precipitation of VLDL and IDL, but not LDL or HDL. The Kd of the CRP/VLDL interaction is 340 nM, and the IC50 for Ca++ is 5.0 mM. In 15 plasmas with the BPW, CRP was highly elevated (77-398 mug/mL), and the concentration of isolated VLDL ranged from 0.082 to 1.32 mM (cholesterol). The turbidity change on recalcification correlates well with the calculated level of the CRP-VLDL complex. Clinically, the BPW better predicts for DIC than either CRP or triglyceride alone. The complex may have pathophysiological implications because CRP can be detected in the VLDL fraction from sera of patients with the BPW, and the VLDL fraction has enhanced prothrombinase surface activity. The complex has been designated lipoprotein complexed C-reactive protein.

L5 ANSWER 4 OF 5 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN
2001:541497 Document No.: PREV200100541497. Inflammation, not hyperhomocysteinemia, is related to oxidative stress and hemostatic and endothelial dysfunction in uremia. Mezzano, Diego [Reprint author]; Pais, Edgar O.; Aranda, Eduardo; Panes, Olga; Downey, Patricio; Ortiz, Mireya; Tagle, Rodrigo; Gonzalez, Fernando; Quiroga, Teresa; Caceres, M. Soledad; Leighton, Federico; Pereira, Jaime. Hemostasis and Thrombosis Laboratory, School of Medicine, Catholic University of Chile, Santiago, Chile. dmezzano@med.puc.cl. Kidney International, (November, 2001) Vol. 60, No. 5, pp. 1844-1850. print.
CODEN: KDYIA5. ISSN: 0085-2538. Language: English.

AB Background. Several cardiovascular risk factors are present in patients with chronic renal failure (CRF), among which are systemic inflammation and hyperhomocysteinemia. Increased oxidative stress, endothelial activation/dysfunction, and coagulation activation are considered integral components of the inflammatory response, but have also been proposed as mediators of plasma homocysteine (tHcy)-induced cell damage. Using correlation analysis, we assessed the relative contributions of inflammation and hyperhomocysteinemia in the abnormal oxidative stress, endothelial activation/dysfunction, and hemostasis activation in patients with CRF. Methods. The relationships of inflammatory proteins and tHcy with plasma markers of these processes were studied in 64 patients with CRF (serum creatinine 526 +- 319 mumol/L) on conservative treatment, comparing the results with healthy controls (N = 15 to 40, depending on

the measured variable) of similar sex and age. Results. Patients had significant increases in inflammatory cytokines (TNF-alpha and IL-8) and acute-phase proteins (C-reactive protein, fibrinogen and alpha1-antitrypsin). tHcy was increased in 87.5% of patients (mean = 27.1 mumol/L, range 6.5 to 118). Patients had significant increases in (1) indices of oxidative stress: TBARS (thiobarbituric acid-reactive species), a marker of lipid peroxidation and AOPP (advanced oxidation protein products), a marker of protein oxidation; (2) endothelial cell markers such as von Willebrand factor (vWF:Ag), soluble ICAM-1 and soluble thrombomodulin (sTM); (3) markers of intravascular thrombin generation: thrombin-antithrombin complexes (TAT) and prothrombin fragment F1+2 (PF1+2); and (4) indices of activation of fibrinolysis: plasmin-antiplasmin complexes (PAP), fibrin degradation products (FnDP) and fibrinogen degradation products (FgDP). tHcy was significantly correlated with plasma creatinine ($r = 0.29$, $P < 0.018$) and with serum folate ($r = -0.38$, $P < 0.002$). However, no significant correlations were observed between tHcy and TBARS, AOPP, vWF:Ag, sICAM-1, sTM, TAT, F1+2, sTF, PAP, FnDP, and FgDP. Conversely, acute-phase proteins showed significant, positive correlations with most markers of oxidative stress, endothelial dysfunction and hemostatic activation. Conclusions. Systemic inflammation, which is closely associated with augmented oxidative stress, endothelial cell dysfunction and hemostatic activation, emerges as a major cardiovascular risk factor in CRF. tHcy is unrelated to these events. Thus, alternative mechanisms through which hyperhomocysteinemia could predispose to vascular lesion and thrombotic events in CRF needs to be investigated.

L5 ANSWER 5 OF 5 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN
2001:305605 Document No.: PREV200100305605. The value of the APTT waveform in predicting mortality and haemostatic dysfunction. Toh, Cheng-Hock [Reprint author]; Downey, Colin [Reprint author]; Wenstone, Richard [Reprint author]; Paton, Ray [Reprint author]; Ticknor, Larry. Haematology, Anaesthesia and Computer Science, University of Liverpool, Liverpool, USA. Blood, (November 16, 2000) Vol. 96, No. 11 Part 1, pp. 51a. print.
Meeting Info.: 42nd Annual Meeting of the American Society of Hematology. San Francisco, California, USA. December 01-05, 2000. American Society of Hematology.
CODEN: BLOOAW. ISSN: 0006-4971. Language: English.

AB The molecular mechanism underlying the biphasic APTT waveform, which is detected in patients with haemostatic dysfunction, has now been unravelled. This is due to a complex between very low or intermediate density lipoprotein and C-reactive protein (CRP) that is induced by calcium ions. An immediate, progressive drop from 100% light transmittance occurs and the degree of this change at 18 seconds (TL18) can be quantified on the MDA-180 automated haemostasis analyser. The clinical ramifications of lipoprotein complexed-CRP formation have now been further examined in the intensive care unit (ICU) setting. Over a 24-month period, 1187 consecutive patients admitted into the ICU were monitored through daily APTT waveform analysis. On admission, 242 patients exhibited a biphasic waveform with 370 others developing biphasic changes subsequently. Biphasic waveforms on admission were associated with the positive predictive value (PPV) for death of 52% as compared with 31% for all unscreened admissions. When the most severe change in the biphasic slope was correlated with outcome by selecting the lowest TL18 in any one patient, the association was even more striking. Data analysed by non-linear regression, showed a stepwise increase in mortality. The PPV for DIC also increased similarly although deaths in the 90 to 100% TL18 ranges were not predicted through the presence of overt DIC (Japanese MHW 1988 score). However, all deaths in this group had evidence of haemostatic dysfunction with elevated markers of thrombin generation. Conclusion: The APTT waveform can identify ICU patients at risk of an adverse outcome both on and during admission. It has the potential too of shedding light on the pathophysiological interactions between coagulation, inflammation and the lipid response.

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=> d his

     (FILE 'HOME' ENTERED AT 09:56:43 ON 06 JUL 2006)

     FILE 'MEDLINE, EMBASE, BIOSIS, SCISEARCH, CAPLUS' ENTERED AT 09:57:14 ON
     06 JUL 2006
L1      4295595 S COMPLEX
L2           17 S L1 AND HEMOSTATIC DYSFUNCTION
L3            5 S L2 AND "C-REACTIVE PROTEIN"
L4            1 S L3 AND VLDL
L5            5 DUP REMOVE L3 (0 DUPLICATES REMOVED)

=> s l2 and c-reactive protein
L6            5 L2 AND C-REACTIVE PROTEIN

=> s l6 and IDL
L7            1 L6 AND IDL

=> d l7 cbib abs

L7   ANSWER 1 OF 1  BIOSIS  COPYRIGHT (c) 2006 The Thomson Corporation  on STN
2002:541408  Document No.: PREV200200541408. Biphasic transmittance waveform in
     the APTT coagulation assay is due to the formation of a Ca++-dependent
     complex of C-reactive protein with
     very-low-density lipoprotein and is a novel marker of impending
     disseminated intravascular coagulation. Toh, Cheng Hock; Samis, John;
     Downey, Colin; Walker, John; Becker, Lev; Brufatto, Nicole; Tejidor,
     Liliana; Jones, Greg; Houdijk, Wim; Giles, Alan; Koschinsky, Marlys;
     Ticknor, Larry O.; Paton, Ray; Wenstone, Richard; Nesheim, Michael
     [Reprint author]. Department of Biochemistry, Queen's University,
     Botterell Hall, Room A210, Kingston, ON, K7L 3N6, Canada.
     nesheimm@post.queensu.ca. Blood, (October 1, 2002) Vol. 100, No. 7, pp.
     2522-2529. print.
     CODEN: BLOOAW. ISSN: 0006-4971. Language: English.
AB   A decrease in light transmittance before clot formation, manifesting as a
     biphasic waveform (BPW) pattern in coagulation assays, was previously
     correlated with the onset of disseminated intravascular coagulation (DIC).
     In this study of 1187 consecutive admissions to the intensive care unit,
     the degree of this change on admission predicts DIC better than D-dimer
     measurements.  Additionally, the BPW preceded the time of DIC diagnosis by
     18 hours, on average, in 56% (203 of 362) of DIC patients.  The BPW is due
     to the rapid formation of a precipitate and coincident turbidity change on
     recalcification of plasma.  The isolated precipitate contains
     very-low-density lipoprotein (VLDL) and C-reactive
     protein (CRP).  The addition of CRP and Ca++ to normal plasma also
     causes the precipitation of VLDL and IDL, but not LDL or HDL.
     The Kd of the CRP/VLDL interaction is 340 nM, and the IC50 for Ca++ is 5.0
     mM.  In 15 plasmas with the BPW, CRP was highly elevated (77-398 mug/mL),
     and the concentration of isolated VLDL ranged from 0.082 to 1.32 mM
     (cholesterol).  The turbidity change on recalcification correlates well
     with the calculated level of the CRP-VLDL complex.  Clinically,
     the BPW better predicts for DIC than either CRP or triglyceride alone.
     The complex may have pathophysiological implications because CRP
     can be detected in the VLDL fraction from sera of patients with the BPW,
     and the VLDL fraction has enhanced prothrombinase surface activity.  The
     complex has been designated lipoprotein complexed C-
     reactive protein.


=> dup remove l2
PROCESSING COMPLETED FOR L2
L8           10 DUP REMOVE L2 (7 DUPLICATES REMOVED)

=> d l8 1-10 cbib abs
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L8 ANSWER 1 OF 10 CAPLUS COPYRIGHT 2006 ACS on STN
2006:538913 Document No. 145:23858 Method for diagnosing critically ill patients by measuring the formation of lipoprotein-C-reactive protein complex in the presence of a surfactant. Jones, Gregory Ray; Borzhemskaya, Larisa; Hanson, Donald G.; Estevez, Rafael Angel; Wilson, Mark S.; Link, John Glenn; Barnes, Bryan (Biomerieux, Inc., USA). PCT Int. Appl. WO 2006060386 A1 20060608, 37 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IS, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2005-US43120 20051130. PRIORITY: US 2004-632431P 20041201.

AB Provided is an improved method of diagnosing and monitoring hemostatic dysfunction, sepsis-related morbidity or severe infection by improving detection of an in vitro complex formed by lipoprotein and C-reactive protein with the utilization of an effective amount of a surface active agent in the reagent. The method includes: (a) obtaining a patient sample; (b) combining said sample with a reagent comprising a divalent cation and an effective amount of a surface active agent to form a reaction mixture; and (c) examining said reaction mixture to determine whether an LC-CRP complex is formed to diagnose or monitor patients having hemostatic dysfunction, sepsis-related morbidity or severe infection.

L8 ANSWER 2 OF 10 MEDLINE on STN DUPLICATE 1
2005257477. PubMed ID: 15891336. Effects of tempol, a free radical scavenger, on long-term hyperdynamic porcine bacteremia. Matejovic Martin; Krouzecky Ales; Martinkova Vendula; Rokyta Richard Jr; Radej Jaroslav; Kralova Hana; Treska Vladislav; Radermacher Peter; Novak Ivan. (Intensive Care Unit, First Medical Department, Charles University Medical School and Teaching Hospital, Plzen, Czech Republic.) Critical care medicine, (2005 May) Vol. 33, No. 5, pp. 1057-63. Journal code: 0355501. ISSN: 0090-3493. Pub. country: United States. Language: English.

AB OBJECTIVES: Pretreatment with tempol, a membrane-permeable radical scavenger, has been shown to be protective in rodent models of endotoxic and Gram-positive shock. However, neither the pretreatment design nor hypodynamic endotoxic shock in rodents mimics the clinical scenario. Therefore, we investigated the effects of tempol in a posttreatment model of long-term, volume-resuscitated, hyperdynamic porcine bacteremia. DESIGN: Prospective, randomized, controlled experimental study. SETTING: University animal laboratory. SUBJECTS: Sixteen anesthetized, mechanically ventilated, and instrumented pigs. INTERVENTIONS: Sepsis was induced and maintained for 24 hrs with continuous infusion of live Pseudomonas aeruginosa. After 12 hrs of hyperdynamic sepsis, animals were randomized to receive either vehicle (control, n = 8) or continuous infusion of tempol (n = 8, 30 mg/kg/hr). MEASUREMENTS AND MAIN RESULTS: Systemic and hepatosplanchnic hemodynamics, oxygen exchange, metabolism, ileal mucosal microcirculation, and tonometry as well as oxidative stress and coagulation variables were assessed before and after 12, 18, and 24 hrs of P. aeruginosa infusion. Tempol significantly attenuated reduction in mean arterial pressure. Despite comparable mesenteric macrocirculation, tempol attenuated the otherwise progressive deterioration in ileal mucosal microcirculation and prevented mucosal acidosis. By contrast, treatment with tempol failed to influence the P. aeruginosa-induced derangements of hepatosplanchnic redox state, liver lactate clearance, and regional acidosis but prevented the development of renal dysfunction. In addition, tempol reduced nitrosative stress without significant effect on the gradual increase in plasma 8-isoprostanes. Finally, tempol attenuated sepsis-induced endothelial (von Willebrand

factor) and hemostatic dysfunction (thrombin-antithrombin complexes, plasminogen activator inhibitor-type 1). CONCLUSIONS: The radical scavenger tempol partially prevented live bacteria from causing key features of hemodynamic and metabolic derangements in porcine hyperdynamic sepsis and beneficially affected surrogate markers of sepsis-induced endothelial and coagulation dysfunction. Incomplete reduction of oxidative stress because of dilutional effects and/or missed optimal therapeutic window for antioxidant treatment when used in posttreatment approach may account for the only partial protection by tempol in this model.

L8 ANSWER 3 OF 10 EMBASE COPYRIGHT (c) 2006 Elsevier B.V. All rights reserved on STN

2005440467 EMBASE A case of reversible posterior leukoencephalopathy syndrome caused by transient hypercoagulable state induced by infection. Yano Y.; Kario K.; Fukunaga T.; Ohshita T.; Himeji D.; Yano M.; Nakagawa S.; Sakata Y.; Shimada K.. Dr. Y. Yano, Department of Internal Medicine, Nango National Health Insurance Hospital, Ohaza Mikado 1078, Nango Village, Miyazaki 883-0306, Japan. yyano@jichi.jp. Hypertension Research Vol. 28, No. 7, pp. 619-623 2005.
Refs: 27.
ISSN: 0916-9636. CODEN: HRESE4
Pub. Country: Japan. Language: English. Summary Language: English.
Entered STN: 20051020. Last Updated on STN: 20051020

AB We report a normotensive case of reversible posterior leukoencephalopathy syndrome caused by transient hypercoagulable state. Hypertension is the main risk factor for reversible posterior leukoencephalopathy syndrome, which is believed to occur as a result of high blood pressure-related dysfunction of cerebrovascular endothelial cells, because it commonly appears in hypertensive emergency. However, in this completely normotensive case, the typical clinical findings of reversible posterior leukoencephalopathy syndrome were triggered by transient hypercoagulable state without any blood pressure variation. The case was successfully treated with anticoagulation therapy using heparin. Thus, this case indicates that reversible posterior leukoencephalopathy syndrome is induced by cerebrovascular endothelial dysfunction, which is induced not only by high blood pressure but also hemostatic dysfunction.

L8 ANSWER 4 OF 10 SCISEARCH COPYRIGHT (c) 2006 The Thomson Corporation on STN

2004:21509 The Genuine Article (R) Number: 755CR. Coagulation profiles in 27 horses with large colon volvulus. Dallap B L (Reprint); Dolente B; Boston R. Univ Penn, Sch Vet Med, New Bolton Ctr, Dept Clin Studies, 382 W St Rd, Kennett Sq, PA 19348 USA (Reprint); Univ Penn, Sch Vet Med, New Bolton Ctr, Dept Clin Studies, Kennett Sq, PA 19348 USA. JOURNAL OF VETERINARY EMERGENCY AND CRITICAL CARE (DEC 2003) Vol. 13, No. 4, pp. 215-225. ISSN: 1534-6935. Publisher: BLACKWELL PUBL LTD, 108 COWLEY RD, OXFORD OX4 1JF, OXON, ENGLAND. Language: English.
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Objective: The objective of this study was to evaluate coagulation profiles in horses with surgical treatment of large colon volvulus (LCV), and determine if an association exists between hemostatic dysfunction and outcome.

Design: Prospective clinical investigation from February to December 2000.

Setting: Large animal intensive care unit in a veterinary teaching hospital.

Interventions: Blood was collected from horses intra-operatively, 24, and 48 hours following surgical treatment for LCV

Measurements: Coagulation profiles, thrombin-antithrombin (TAT) levels, and D-dimer concentrations were determined for each time point. The number of tests abnormal in the standard coagulation profile, defined as the degree of hemostatic dysfunction, was determined for each horse for the duration of the study period. The

association between each test and outcome, as well as the degree of hemostatic dysfunction for each horse and outcome, was determined using univariate analysis and logistic regression. TAT levels and D-dimer concentrations were compared to the results of the standard coagulation profile and to patient outcome using univariate analysis and logistic regression.

Main results: Seventy percent of horses evaluated with surgical treatment of LCV had evidence of hemostatic dysfunction (3/6 tests abnormal). Only 18% of those patients had clinical signs recognized by the attending clinician as a coagulopathy. There was an association between the development of a coagulopathy and outcome, with horses with 4/6 tests abnormal being more likely to be euthanized, and those with 3/6 tests abnormal having a prolonged hospital stay. Platelet count, prothrombin time, and TAT levels may be helpful in predicting outcome in horses with LCV

Conclusions: Hemostatic function should be evaluated in horses with surgical treatment of LCV to detect subclinical coagulopathies and direct subsequent intervention.

L8 ANSWER 5 OF 10 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN
DUPLICATE 2

2003:511449 Document No.: PREV200300514434. Characterization of thrombin activatable fibrinolysis inhibitor in normal and acquired haemostatic dysfunction. Toh, Cheng Hock [Reprint Author]. Roald Dahl Haemostasis and Thrombosis Centre, Royal Liverpool University Hospital, Liverpool, UK. C.H.toh@liverpool.ac.uk. Blood Coagulation & Fibrinolysis, (June 2003) Vol. 14, No. Supplement 1, pp. S69-S71. print.
CODEN: BLFIE7. ISSN: 0957-5235. Language: English.

AB Thrombin activatable fibrinolysis inhibitor (TAFI) is a carboxypeptidase B-like proenzyme, which is synthesized in the liver and circulates in the blood at a concentration of about 275 nmol/l. Once activated, by thrombin or plasmin, TAFI down regulates fibrinolysis, slowing clot lysis by cleaving the C-terminal lysine and arginine residues from partially degraded fibrin. Thrombomodulin enhances thrombin activation of TAFI by more than 1000-fold, suggesting that the thrombin-thrombomodulin complex is the physiological activator of TAFI. Activated protein C can up-regulate fibrinolysis by limiting the activation of TAFI via the attenuation of thrombin production. While impairment of fibrinolysis may predispose to thrombosis, excessive fibrinolysis may result in a bleeding tendency. In acquired coagulopathies, TAFI antigen levels are reduced in patients with disseminated intravascular coagulation. In focusing on women with major post-partum haemorrhage requiring blood transfusion, a significant reduction in TAFI levels is observed. The precise degree of TAFI activation is currently being characterized using new and more specific assays. The resulting data may provide insight into therapeutic options to treat post-partum haemorrhage, which is associated with significant morbidity.

L8 ANSWER 6 OF 10 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN

2002:541408 Document No.: PREV200200541408. Biphasic transmittance waveform in the APTT coagulation assay is due to the formation of a Ca++-dependent complex of C-reactive protein with very-low-density lipoprotein and is a novel marker of impending disseminated intravascular coagulation. Toh, Cheng Hock; Samis, John; Downey, Colin; Walker, John; Becker, Lev; Brufatto, Nicole; Tejidor, Liliana; Jones, Greg; Houdijk, Wim; Giles, Alan; Koschinsky, Marlys; Ticknor, Larry O.; Paton, Ray; Wenstone, Richard; Nesheim, Michael [Reprint author]. Department of Biochemistry, Queen's University, Botterell Hall, Room A210, Kingston, ON, K7L 3N6, Canada. nesheimm@post.queensu.ca. Blood, (October 1, 2002) Vol. 100, No. 7, pp. 2522-2529. print.
CODEN: BLOOAW. ISSN: 0006-4971. Language: English.

AB A decrease in light transmittance before clot formation, manifesting as a biphasic waveform (BPW) pattern in coagulation assays, was previously correlated with the onset of disseminated intravascular coagulation (DIC). In this study of 1187 consecutive admissions to the intensive care unit,

the degree of this change on admission predicts DIC better than D-dimer measurements. Additionally, the BPW preceded the time of DIC diagnosis by 18 hours, on average, in 56% (203 of 362) of DIC patients. The BPW is due to the rapid formation of a precipitate and coincident turbidity change on recalcification of plasma. The isolated precipitate contains very-low-density lipoprotein (VLDL) and C-reactive protein (CRP). The addition of CRP and Ca++ to normal plasma also causes the precipitation of VLDL and IDL, but not LDL or HDL. The Kd of the CRP/VLDL interaction is 340 nM, and the IC50 for Ca++ is 5.0 mM. In 15 plasmas with the BPW, CRP was highly elevated (77-398 mug/mL), and the concentration of isolated VLDL ranged from 0.082 to 1.32 mM (cholesterol). The turbidity change on recalcification correlates well with the calculated level of the CRP-VLDL complex. Clinically, the BPW better predicts for DIC than either CRP or triglyceride alone. The complex may have pathophysiological implications because CRP can be detected in the VLDL fraction from sera of patients with the BPW, and the VLDL fraction has enhanced prothrombinase surface activity. The complex has been designated lipoprotein complexed C-reactive protein.

L8 ANSWER 7 OF 10 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN
2001:541497 Document No.: PREV200100541497. Inflammation, not hyperhomocysteinemia, is related to oxidative stress and hemostatic and endothelial dysfunction in uremia. Mezzano, Diego [Reprint author]; Pais, Edgar O.; Aranda, Eduardo; Panes, Olga; Downey, Patricio; Ortiz, Mireya; Tagle, Rodrigo; Gonzalez, Fernando; Quiroga, Teresa; Caceres, M. Soledad; Leighton, Federico; Pereira, Jaime. Hemostasis and Thrombosis Laboratory, School of Medicine, Catholic University of Chile, Santiago, Chile. dmezzano@med.puc.cl. Kidney International, (November, 2001) Vol. 60, No. 5, pp. 1844-1850. print.
CODEN: KDYIA5. ISSN: 0085-2538. Language: English.

AB Background. Several cardiovascular risk factors are present in patients with chronic renal failure (CRF), among which are systemic inflammation and hyperhomocysteinemia. Increased oxidative stress, endothelial activation/dysfunction, and coagulation activation are considered integral components of the inflammatory response, but have also been proposed as mediators of plasma homocysteine (tHcy)-induced cell damage. Using correlation analysis, we assessed the relative contributions of inflammation and hyperhomocysteinemia in the abnormal oxidative stress, endothelial activation/dysfunction, and hemostasis activation in patients with CRF. Methods. The relationships of inflammatory proteins and tHcy with plasma markers of these processes were studied in 64 patients with CRF (serum creatinine 526 +- 319 mumol/L) on conservative treatment, comparing the results with healthy controls (N = 15 to 40, depending on the measured variable) of similar sex and age. Results. Patients had significant increases in inflammatory cytokines (TNF-alpha and IL-8) and acute-phase proteins (C-reactive protein, fibrinogen and alpha1-antitrypsin). tHcy was increased in 87.5% of patients (mean = 27.1 mumol/L, range 6.5 to 118). Patients had significant increases in (1) indices of oxidative stress: TBARS (thiobarbituric acid-reactive species), a marker of lipid peroxidation and AOPP (advanced oxidation protein products), a marker of protein oxidation; (2) endothelial cell markers such as von Willebrand factor (vWF:Ag), soluble ICAM-1 and soluble thrombomodulin (sTM); (3) markers of intravascular thrombin generation: thrombin-antithrombin complexes (TAT) and prothrombin fragment F1+2 (PF1+2); and (4) indices of activation of fibrinolysis: plasmin-antiplasmin complexes (PAP), fibrin degradation products (FnDP) and fibrinogen degradation products (FgDP). tHcy was significantly correlated with plasma creatinine ($r = 0.29$, $P < 0.018$) and with serum folate ($r = -0.38$, $P < 0.002$). However, no significant correlations were observed between tHcy and TBARS, AOPP, vWF:Ag, sICAM-1, sTM, TAT, F1+2, sTF, PAP, FnDP, and FgDP. Conversely, acute-phase proteins showed significant, positive correlations with most markers of oxidative stress, endothelial dysfunction and hemostatic activation. Conclusions. Systemic inflammation, which is closely associated with augmented oxidative stress, endothelial cell dysfunction and hemostatic activation, emerges as a major

cardiovascular risk factor in CRF. tHcy is unrelated to these events. Thus, alternative mechanisms through which hyperhomocysteinemia could predispose to vascular lesion and thrombotic events in CRF needs to be investigated.

L8 ANSWER 8 OF 10 CAPLUS COPYRIGHT 2006 ACS on STN
2001:307745 Document No. 135:73382 Thromboplastin sensitivity in waveform analysis. Toh, Cheng Hock; Downey, Colin; Dwyre, Louise (Department of Haematology, Royal Liverpool University Hospital, Liverpool, L78XP, UK). Thrombosis and Haemostasis, 84(3), 517-518 (English) 2000. CODEN: THHADQ. ISSN: 0340-6245. Publisher: F. K. Schattauer Verlagsgesellschaft mbH.
AB The waveform anal. charts light transmittance changes over the course and duration of clot formation in simple assays of coagulation. In patients with coagulopathies, the normal sigmoidal waveform profile on the activated partial thromboplastin time (APTT) assay. This study has therefore shown that with the choice of particular thromboplastins in a diagnostic laboratory, the screening capacity of waveform anal. for unsuspected hemostatic dysfunction can be extended to the PT assay.
We have shown that mild biphasic slopes can be detected in patients with atrial fibrillation, a condition where many are on anticoagulant prophylaxis against thrombotic stroke. Finally, this observation of thromboplastin difference also adds considerable insight into the mechanism underlying the biphasic waveform; the unraveling of which promises to provide further information on the often complex pathophysiol. changes in these clin. conditions.

L8 ANSWER 9 OF 10 MEDLINE on STN DUPLICATE 3
2001109123. PubMed ID: 10946808. Haemostatic changes in systemic inflammatory response syndrome during continuous renal replacement therapy. Garcia-Fernandez N; Lavilla F J; Rocha E; Purroy A. (Dept. of Nephrology, University Clinic of Navarra, School of Medicine, University of Navarra, Pamplona, Spain.) Journal of nephrology, (2000 Jul-Aug) Vol. 13, No. 4, pp. 282-9. Journal code: 9012268. ISSN: 1121-8428. Pub. country: Italy. Language: English.
AB BACKGROUND: Endothelial damage and hemostatic imbalance play an important role in the evolution of the Systemic Inflammatory Response Syndrome (SIRS) into the Multiple Organ Dysfunction Syndrome (MODS). In Acute Renal Failure associated with SIRS, different types of Continuous Renal Replacement Therapies (CRRT) may give non-renal benefits by modifying the levels of some factors related to those disturbances. METHODS: Forty patients with SIRS-associated ARF were randomised to receive either continuous venovenous hemofiltration (CVVH) or continuous venovenous hemodiafiltration (CVVHDF) for the first 24 h. Afterwards the CRRT method was reversed. The group treated with CVVH moved to CVVHDF and that treated with CVVHDF to CVVH for the next 24 h. Plasma levels of: von Willebrand Factor (vWF), thrombomodulin, plasminogen activity inhibitor type 1 (PAI-1: antigen and activity), tissue type plasminogen activator (t-PA: antigen), prothrombin fragment 1+2 (F1+2) and thrombin-antithrombin complexes (TAT) were measured previously to CRRT (base-line), and after 24 and 48 hours of therapy. Multivariate ANOVA was the statistical method used. RESULTS: In the MANOVA study a significant decrease in PAI-1 activity during the treatment procedure was observed (horizontality $p < 0.05$). PAI-1 antigen showed a tendency to decrease although without statististical significance. There were no significantly different changes in the other factors analysed during either CRRT (parallelism $p > 0.05$). At the base-line point, all the factors were higher than normal values in healthy adults. CONCLUSIONS: The present study suggests that CRRT, in patients with SIRS, may promote a decrease in PAI-1 and consequently, a better outcome. There were no differences between the CVVH and the CVVHDF methods regarding the factors analysed. The present data confirms that there is an important endothelial and hemostatic dysfunction in SIRS from the early phases.

L8 ANSWER 10 OF 10 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN

2001:305605 Document No.: PREV200100305605. The value of the APTT waveform in predicting mortality and haemostatic dysfunction. Toh, Cheng-Hock [Reprint author]; Downey, Colin [Reprint author]; Wenstone, Richard [Reprint author]; Paton, Ray [Reprint author]; Ticknor, Larry. Haematology, Anaesthesia and Computer Science, University of Liverpool, Liverpool, USA. Blood, (November 16, 2000) Vol. 96, No. 11 Part 1, pp. 51a. print. Meeting Info.: 42nd Annual Meeting of the American Society of Hematology. San Francisco, California, USA. December 01-05, 2000. American Society of Hematology.
CODEN: BLOOAW. ISSN: 0006-4971. Language: English.

AB The molecular mechanism underlying the biphasic APTT waveform, which is detected in patients with haemostatic dysfunction, has now been unravelled. This is due to a complex between very low or intermediate density lipoprotein and C-reactive protein (CRP) that is induced by calcium ions. An immediate, progressive drop from 100% light transmittance occurs and the degree of this change at 18 seconds (TL18) can be quantified on the MDA-180 automated haemostasis analyser. The clinical ramifications of lipoprotein complexed-CRP formation have now been further examined in the intensive care unit (ICU) setting. Over a 24-month period, 1187 consecutive patients admitted into the ICU were monitored through daily APTT waveform analysis. On admission, 242 patients exhibited a biphasic waveform with 370 others developing biphasic changes subsequently. Biphasic waveforms on admission were associated with the positive predictive value (PPV) for death of 52% as compared with 31% for all unscreened admissions. When the most severe change in the biphasic slope was correlated with outcome by selecting the lowest TL18 in any one patient, the association was even more striking. Data analysed by non-linear regression, showed a stepwise increase in mortality. The PPV for DIC also increased similarly although deaths in the 90 to 100% TL18 ranges were not predicted through the presence of overt DIC (Japanese MHW 1988 score). However, all deaths in this group had evidence of haemostatic dysfunction with elevated markers of thrombin generation. Conclusion: The APTT waveform can identify ICU patients at risk of an adverse outcome both on and during admission. It has the potential too of shedding light on the pathophysiological interactions between coagulation, inflammation and the lipid response.

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=> s l1 and serum amyloid A
L9          424 L1 AND SERUM AMYLOID A

=> s l9 and VLDL
L10           0 L9 AND VLDL

=> s l9 and IDL
L11           0 L9 AND IDL

=> s VLDL complex
L12          58 VLDL COMPLEX

=> s l12 and amyloid A
L13           0 L12 AND AMYLOID A

=> s IDL
L14        5460 IDL

=> s l14 and complex
L15         298 L14 AND COMPLEX

=> s l15 and amyloid A
L16           0 L15 AND AMYLOID A

=> s serum amyloid A complex
L17          13 SERUM AMYLOID A COMPLEX
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=> dup remove l17
PROCESSING COMPLETED FOR L17
L18 10 DUP REMOVE L17 (3 DUPLICATES REMOVED)

=> d l18 1-10 cbib abs

L18 ANSWER 1 OF 10 CAPLUS COPYRIGHT 2006 ACS on STN
2004:775364 Document No. 142:334075 A serum amyloid A and LDL complex as a new prognostic marker in stable coronary artery disease. [Erratum to document cited in CA141:069446]. Ogasawara, Ken; Mashiba, Shinichi; Wada, Youichiro; Sahara, Makoto; Uchida, Kazuo; Aizawa, Tadanori; Kodama, Tatsuhiko (The Cardiovascular Institute, Tokyo, 106-0032, Japan). Atherosclerosis (Amsterdam, Netherlands), 176(2), 431 (English) 2004. CODEN: ATHSBL. ISSN: 0021-9150. Publisher: Elsevier B.V..
AB The corrected version of Figure 3 is given.

L18 ANSWER 2 OF 10 CAPLUS COPYRIGHT 2006 ACS on STN
2004:386034 Document No. 141:69446 A serum amyloid A and LDL complex as a new prognostic marker in stable coronary artery disease. Ogasawara, Ken; Mashiba, Shinichi; Wada, Youichiro; Sahara, Makoto; Uchida, Kazuo; Aizawa, Tadanori; Kodama, Tatsuhiko (The Cardiovascular Institute, Tokyo, Minato-ku, 106-0032, Japan). Atherosclerosis (Amsterdam, Netherlands), 174(2), 349-356 (English) 2004. CODEN: ATHSBL. ISSN: 0021-9150. Publisher: Elsevier.
AB Although some reports have indicated that acute phase proteins such as C-reactive protein (CRP) and serum amyloid A (SAA) can predict the prognosis in patients with acute coronary syndrome, the value of these markers in patients with stable coronary artery disease (CAD) still remains obscure. Therefore, our aim was to determine the prognostic value of inflammatory markers in patients with stable coronary artery disease. We conducted a prospective cohort study in 140 consecutive patients with stable coronary artery disease who had at least 1 coronary stenosis more than 50% in diameter seen on diagnostic coronary angiog. (CAG). We determined serum levels of the SAA/LDL complex as a new marker in addition to CRP and SAA. Serum levels of the SAA/LDL complex were measured by a sandwich ELISA. End-points were defined as cardiac death, myocardial infarction, cerebral infarction, and coronary revascularization. End-point events occurred in 21 patients (2 death from myocardial infarction, 2 cerebral infarction, and 17 revascularization). Age (year) (OR = 1.14, CI: 1.05-1.25), diabetes mellitus (OR = 3.50, CI: 1.08-11.40), triglyceride (10 mg/dL) (OR = 1.12, CI: 1.01-1.23) and SAA/LDL complex (10 μg/mL) (OR = 2.32, CI: 1.05-4.70) were independently related to the events. A reconstitution experiment suggested that the SAA/LDL complex is derived by oxidative interaction between SAA and lipoproteins. The SAA/LDL complex reflects intravascular inflammation directly and can be a new marker more sensitive than CRP or SAA for prediction of prognosis in patients with stable coronary artery disease.

L18 ANSWER 3 OF 10 CAPLUS COPYRIGHT 2006 ACS on STN
2004:112006 Document No. 140:195527 Development of blood examination method of serum amyloid A and LDL complex, and clinical application to prediction of cardiovascular event. Mashiba, Shinichi; Ogasawara, Ken; Takeya, Motohiro; Wada, Youichiro; Sahara, Makoto; Kojima, Shiho; Tabata, Kazue; Ueda, Masashi; Uchida, Kazuo; Aizawa, Tadanori; Kodama, Tatsuhiko (Kyoto Med. Sci. Lab., Kyoto, 612-8486, Japan). Rinsho Byori, 52(1), 67-74 (Japanese) 2004. CODEN: RBYOAI. ISSN: 0047-1860. Publisher: Nippon Rinsho Kensa Igakkai.
AB A review. In recent years, it has been reported that the acute-phase proteins C-reactive protein (CRP) and serum amyloid A (SAA), the sera levels of which are elevated in inflammation, are also elevated in coronary artery disease such as acute myocardial infarction. Also, high-sensitivity CRP assay is thought to be useful in predicting the prognosis of coronary heart disease. While investigating complexes of acute-phase proteins and low-d. lipoprotein (LDL), we found a complex of LDL and SAA (SAA/LDL complex). The SAA/LDL complex in blood are formed

from LDL and HDL by an oxidation reaction. Therefore, we developed an ELISA using anti-human SAA antibody and antihuman apoB, and determined a new method for measuring SAA/LDL complex in sera. We evaluated SAA/LDL complex as a new marker for prediction of prognosis in addition to the ordinary markers in consecutive 140 patients with stable coronary heart disease who had at least 1 coronary artery stenosis more than 50% in diameter at the diagnostic coronary angiog. Of these 140 patients, 2 developed fatal myocardial infarction, 2 cerebral infarction, and 17 angina pectoris requiring coronary revascularization therapy during 1 yr and 6 mo after blood examns. The SAA/LDL complex value in the EVENT group of 21 patients was significantly higher than that in the control group of 119 individuals. High-sensitivity CRP (hs-CRP) assay and SAA measurement showed no significant difference between the 2 groups. The SAA/LDL complex reflects intravascular inflammation directly and can be a new marker more sensitive than hs-CRP or SAA for prediction of prognosis in patients with stable coronary artery disease.

L18 ANSWER 4 OF 10 CAPLUS COPYRIGHT 2006 ACS on STN
2001:228722 Document No. 134:265155 Utilization of FPRL1 as a functional receptor by serum amyloid A (SAA) and therapeutic uses thereof. Wang, Ji-Ming; Oppenheim, Joost J.; Su, Shao-Bo; Gong, Wang-Hua; Gao, Ji-Liang; Murphy, Philip M. (Government of the United States of America, as Represented by the Secretary, Department of Health and Human Services, USA). PCT Int. Appl. WO 2001021188 A1 20010329, 141 pp. DESIGNATED STATES: W: AU, CA, US. (English). CODEN: PIXXD2. APPLICATION: WO 1999-US21770 19990922.

AB The present invention relates to the discovery that serum amyloid A (SAA) is a ligand for the FPRL 1 receptor. Disclosed herein, are novel biol. tools for the study of SAA/FPRL1 complex assembly and prophylactics, therapeutics, and methods of use of the foregoing, which modulate the association of SAA with FPRL1 and thereby effect responses including, but not limited to, signal transduction, chemotaxis, leukocyte migration, immune system response, amyloidosis, inflammatory response, infection, organ rejection, arthritis, atherosclerosis, and neoplasia.

L18 ANSWER 5 OF 10 CAPLUS COPYRIGHT 2006 ACS on STN
2001:62437 Document No. 134:97520 Method for detecting low density lipoprotein (LDL) or denatured LDL in blood. Uchida, Kazuo; Mashiba, Shinichi (Ikagaku Co., Ltd., Japan). Eur. Pat. Appl. EP 1070962 A2 20010124, 23 pp. DESIGNATED STATES: R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO. (English). CODEN: EPXXDW. APPLICATION: EP 2000-114984 20000720. PRIORITY: JP 1999-207913 19990722; JP 2000-12210 20000120.

AB A novel method for detecting LDL and denatured LDL (particularly, oxidized LDL) having a significant concern with the onset and progression of arteriosclerosis and Alzheimer's disease is provided, wherein a complex of denatured LDL (particularly, oxidized LDL) with an acute phase reactant, blood coagulation-fibrinolytic-related protein or disinfectant substance produced by macrophage is used as a measuring subject. Human LDL free of α1 antitrypsin and human fibronectin were treated with a copper sulfate solution at 37° over night to form an oxidized LDL-fibronectin complex. The complex was used as an immunogen in a mouse from which monoclonal antibodies were prepared for use in assaying for the complex.

L18 ANSWER 6 OF 10 CAPLUS COPYRIGHT 2006 ACS on STN
1998:343512 Document No. 130:51263 Comparison of the binding and endocytosis of high-density lipoprotein from healthy (HDL) and inflamed (HDLSAA) donors by murine macrophages of four different mouse strains. Rocken, C.; Kisilevsky, Robert (Queen's University and The Syl and Molly Apps Medical Research Centre, Department of Pathology, Kingston General Hospital, Kingston, ON, K7L 3N6, Can.). Virchows Archiv, 432(6), 547-555 (English) 1998. CODEN: VARCEM. ISSN: 0945-6317. Publisher: Springer-Verlag.

AB Serum amyloid A (SAA) is a plasma acute phase protein and the precursor of the AA-fibril protein deposited in AA-amyloidosis. SAA is bound mainly to high-d. lipoproteins (HDLSAA). Previous investigations have demonstrated

that peritoneal macrophages (mϕ) from mice are capable of binding and endocytosing HDLSAA. This observation may indicate a pathway by which SAA enters the mϕ and where its intracellular metabolism may be followed by degradation and/or amyloidogenesis. Since binding and internalization defects of lipoproteins may be associated with different diseases, it is possible that mouse strain susceptibility to amyloidosis is associated with qual. differences in the binding and internalization of HDLSAA. To test this hypothesis a series of binding and internalization expts. was performed in vitro with mO from four different mouse strains, CD-1, A/J, C57BL/6J and C3H/HeJ, which differ in their susceptibility to AA-amyloidosis. Using colloidal gold-labeled lipoproteins, it was evident by light and electron microscopy that mϕ from all four mouse strains are capable of binding and internalizing HDL (without SAA) and HDLSAA. HDL and HDLSAA were found in such compartments of the receptor-mediated pathway as coated pits, coated vesicles, endosomes and multivesicular bodies and in lipid droplets; no qual. differences were observed Therefore, it is unlikely that a defect in binding and uptake of HDLSAA is related to the different susceptibilities of these mouse strains to develop AA-amyloidosis. However, the results do not exclude the possibility that differences in the intracellular processing of SAA following endocytosis of HDLSAA is involved in this differing susceptibility.

L18 ANSWER 7 OF 10 CAPLUS COPYRIGHT 2006 ACS on STN
1997:20311 Document No. 126:58825 Binding of human serum amyloid A (hSAA) and its high-density lipoprotein3 complex (hSAA-HDL3) to human neutrophi'ls. Possible implication to the function of a protein of an unknown physiological role. Preciado-Patt, Liana; Pras, Mordechai; Fridkin, Mati (Department of Organic Chemistry, The Weizmann Institute of Science, Rehovot, Israel). International Journal of Peptide & Protein Research, 48(6), 503-513 (English) 1996. CODEN: IJPPC3. ISSN: 0367-8377. Publisher: Munksgaard.
AB Serum amyloid A (SAA) is an acute-phase serum protein which exists in the body in a complex with high-d. lipoprotein (HDL3). It is involved in chronic inflammation and neoplastic diseases in an as yet unknown manner. Toward an understanding of the possible physiol. role of SAA we initiated a study of its association with blood proinflammatory cells with which it may interact functionally in vivo. In the following we describe the binding characteristics of recombinant human SAA to human neutrophils (polymorphonuclear leukocytes; PMNLs) and their plasma membranes. Scatchard anal. of rSAA binding and displacement curves revealed Kd in the nanomolar range. The C-terminal domain of the protein, i.e. amino acid residues 77-104, which might reside in serum following SAA degradation and amyloid A formation, was found to inhibit efficiently the binding of the whole protein to neutrophils. The interaction of SAA, and of its related peptides while complexed in HDL3, with human PMNs was also studied. The results suggest that SAA may be involved, in an as yet unknown manner, in the neutrophil-associated inflammatory mechanism.

L18 ANSWER 8 OF 10 CAPLUS COPYRIGHT 2006 ACS on STN
1996:581244 Document No. 125:298712 Degradation of serum amyloid A in amyloid-susceptible and amyloid-resistant mouse strains. Elliott-Bryant, R.; Liang, J. -S.; Sipe, J. D.; Cathcart, E. S. (Edith Nourse Rogers Memorial Veterans Hospital, Bedford, MA, 01730, USA). Scandinavian Journal of Immunology, 44(3), 223-228 (English) 1996. CODEN: SJIMAX. ISSN: 0300-9475. Publisher: Blackwell.
AB Degradation of serum amyloid A (apoSAA) by resident peritoneal cells (RPCS) and conditioned medium (CDM), prepared with RPCS, from amyloid-susceptible CBA/J mice, amyloid-resistant CE/J mice, and their amyloid-resistant CBA/J + CE/J F1 progeny was investigated in vitro. Serum amyloid A was derived from murine acute phase (AP) plasma and associated with high d. lipoprotein (HDL). Degradation of apoSAA by RPCS and CDM from CBA/J mice was complete while degradation by RPCS and CDM from CE/J mice did not occur. Degradation of apoSAA by RPCS and CDM from CBA/J + CE/J F1 hybrid mice was indistinguishable from that by RPCS and CDM from the CBA/J parent. Intermediate fragments were not detected with either RPCS or CDM from

CBA/J mice or CBA/J + CE/J F1 hybrid mice. Degradation of apoSAA was inhibited by phenylmethanylsulfonyl fluoride (PMSF) indicating that the enzyme, secreted into the fluid phase, was a serine esterase. Unlike apoSAA, HDL-associated apoA-1 remained intact. Thus, while selective degradation of HDL-associated apoSAA (apoSAA-HDL) by RPCS from the CBA/J and CE/J mice was different, the genetic study did not support the hypothesis that there was direct linkage between impaired degradation of apoSAA-HDL in the CE/J mouse strain and protection against amyloid fibril formation. As amyloid resistance in CBA/J + CE/J F1 hybrid mice is not attributable to failure to express the amyloidogenic isoform apoSAA2, the study supports the original hypothesis that amyloid resistance may be linked to expression of apoSAAcej.

L18 ANSWER 9 OF 10 MEDLINE on STN DUPLICATE 1

90089369. PubMed ID: 2512983. Influence of serum amyloid A on cholesterol esterification in human plasma. Steinmetz A; Hocke G; Saile R; Puchois P; Fruchart J C. (Abt. Endokrinologie und Stoffwechsel, Philipps-Universitat Marburg, F.R.G.) Biochimica et biophysica acta, (1989 Nov 28) Vol. 1006, No. 2, pp. 173-8. Journal code: 0217513. ISSN: 0006-3002. Pub. country: Netherlands. Language: English.

AB Lecithin-cholesterol acyltransferase (EC 2.3.1.43, LCAT) is the enzyme responsible for the formation of the bulk of cholesteryl ester in human plasma. The LCAT-reaction takes place mainly on high-density lipoproteins and requires an apolipoprotein as activator. Besides apolipoprotein (apo) A-I several other potent activator apolipoproteins (AIV, E and CI) were identified, furthermore apo A-II was shown to be a modulator of the enzyme's reaction in the presence of apo A-I. Serum amyloid A, an apolipoprotein mainly associated with high-density lipoprotein, massively accumulates in plasma upon acute phase reactions. We therefore studied the possible influence of this acute phase reactant on cholesterol esterification in human plasma. There was a significant decrease of esterified cholesterol in plasma during acute phase reaction. We found a highly significant correlation between the unesterified part of plasma cholesterol and serum amyloid A levels ($r = 0.694$, $P = 0.0001$). Also, plasma LCAT activity was negatively correlated with serum amyloid A levels. Lipoproteins containing apo A-I and A-II (LpA-I: A-II) and lipoproteins containing apo A-I but no A-II (LpA-I) decreased significantly with the appearance in plasma of serum amyloid A. To study the influence of serum amyloid A on the LCAT reaction, artificial substrates were prepared either by a detergent dialysis procedure or by addition of apolipoprotein to a sonicated aqueous dispersion of lipid. In addition two different molar ratios of apolipoprotein/phospholipid (PC) (1:50 and 1:310) were chosen at a constant molar ratio of total cholesterol/PC of 1:20. The various substrates were incubated with purified LCAT enzyme. DMPC - or egg yolk phosphatidylcholine - cholesterol-[4-14C]cholesterol-serum amyloid A complexes per se did not stimulate LCAT activity significantly. However, apo serum amyloid A incorporated together with apo A-I by a detergent dialysis procedure lead at low concentrations of serum amyloid A to a marked increase in cholesteryl ester formation as compared to apo A-I alone but inhibited the cholesteryl ester formation at high concentrations. Thus, the low levels of esterified cholesterol in acute phase plasma are to some extent due to decreased plasma enzyme activity and in part may be due to interference of apo serum amyloid A with the natural substrate complexes of plasma HDL.

L18 ANSWER 10 OF 10 CAPLUS COPYRIGHT 2006 ACS on STN

1987:16566 Document No. 106:16566 Changes in the serum amyloid A protein complex during the acute phase response. Renversez, J. C.; Roussel, S.; Valle, M. J. (Cent. Hosp. Reg. Univ. Grenoble, 38043, Fr.). Protides of the Biological Fluids, 34, 339-42 (English) 1986. CODEN: PBFPA6. ISSN: 0079-7065.

AB Serum amyloid A (SAA) protein had an intrinsic peroxidase activity in an ELISA using peroxidase-labeled antibody. The pre-α fraction of

lipoproteins in inflammatory serums was separated by SDS-PAGE. After reduction, 3
fractions, identified as prealbumin [38 kilodaltons (KD)], retinol-binding protein (23 KD), and SAA (18 KD), were observed Thus, in inflammation, SAA may circulate as very large complexes with other proteins, and these complexes apparently possess peroxidase activity.

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L19 30276 (FISCHER T?/AU OR DOWNEY C?/AU OR NESHEIM M?/AU OR SAMIS J?/AU OR TEJIDOR L?/AU OR TOH C?/AU OR WALKER J?/AU)

=> s l19 and prognosis
L20 255 L19 AND PROGNOSIS

=> s l20 and inflammatory condition
L21 0 L20 AND INFLAMMATORY CONDITION

=> s l20 and inflammation
L22 5 L20 AND INFLAMMATION

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PROCESSING COMPLETED FOR L22
L23 4 DUP REMOVE L22 (1 DUPLICATE REMOVED)

=> d l23 1-4 cbib abs

L23 ANSWER 1 OF 4 MEDLINE on STN
2003498569. PubMed ID: 14576251. Disseminated intravascular coagulation: old disease, new hope. Toh Cheng Hock; Dennis Michael. (Roald Dahl Haemostasis and Thrombosis Centre, Royal Liverpool University Hospital, Liverpool L7 8XP.. toh@liverpool.ac.uk) . BMJ (Clinical research ed.), (2003 Oct 25) Vol. 327, No. 7421, pp. 974-7. Ref: 25. Journal code: 8900488. E-ISSN: 1468-5833. Pub. country: England: United Kingdom. Language: English.

L23 ANSWER 2 OF 4 MEDLINE on STN DUPLICATE 1
2003224139. PubMed ID: 12745654. Current clinical practice. DIC 2002: a review of disseminated intravascular coagulation. Toh Cheng Hock ; Dennis Michael. (Roald Dahl Haemostasis and Thrombosis Centre, Royal Liverpool University Hospital, Liverpool, UK.. toh@liverpool.ac.uk) . Hematology (Amsterdam, Netherlands), (2003 Apr) Vol. 8, No. 2, pp. 65-71. Ref: 51. Journal code: 9708388. ISSN: 1024-5332. Pub. country: England: United Kingdom. Language: English.
AB The turn of the millennium has seen clear advances in the understanding and management of Disseminated Intravascular Coagulation (DIC). The recognition that its pathogenesis stems from sustained thrombin generation in fuelling the cycle between inflammation and coagulation has seen the first successful treatment in severe sepsis through targeting this activity. An advance in treatment brings heightened relevance to laboratory testing, which now emphasises earlier detection and better monitoring to facilitate improved risk-identification and assessment of therapeutic efficacy. This review article also provides insights into future strategies that might build on the foundation of improving prognosis for the patient with DIC.

L23 ANSWER 3 OF 4 SCISEARCH COPYRIGHT (c) 2006 The Thomson Corporation on STN
1994:173377 The Genuine Article (R) Number: MY952. PLASMA-CONCENTRATION OF ELASTASE-ALPHA(1)-PROTEINASE INHIBITOR COMPLEX IN SURFACTANT-TREATED PRETERM NEONATES WITH RESPIRATORY-DISTRESS SYNDROME. TEGTMEYER F K (Reprint); MOLLER J; RICHTER A; WILKEN B; FISCHER T. MED UNIV LUBECK, DEPT PEDIAT, KAHLHORSTSTR 31-35, D-23538 LUBECK, GERMANY (Reprint); MED UNIV LUBECK, DEPT NEONATAL, D-23538 LUBECK, GERMANY; MED

UNIV LUBECK, DEPT ANESTHESIOL, D-23538 LUBECK, GERMANY. EUROPEAN RESPIRATORY JOURNAL (FEB 1994) Vol. 7, No. 2, pp. 260-264. ISSN: 0903-1936 . Publisher: MUNKSGAARD INT PUBL LTD, 35 NORRE SOGADE, PO BOX 2148, DK-1016 COPENHAGEN, DENMARK. Language: English.
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Although exogenous surfactant replacement improves respiratory distress syndrome (RDS) of immature neonates, it may not prevent subsequent lung damage and development of bronchopulmonary dysplasia associated with polymorphonuclear neutrophil (PMN)-activation. We therefore wanted to assess whether surfactant administration would be associated with activation of circulating PMNs.

Since elastase-alpha(1)-proteinase inhibitor (E-alpha(1)-PI) has proved to be a sensitive indicater of intravascular PMN activation, we studied E-alpha(1)-PI plasma concentration in preterm neonates during the treatment of RDS with a bovine surfactant preparation (group I: n=23). Results were compared with those from a retrospective control group treated by ventilation alone (group II: n=13), and with a reference group of 92 newborns (group III).

Following surfactant administration, median E-alpha(1)-PI concentration increased significantly (day 1 80.5 vs Day 2 234 mu g.l(-1)), and exceeded the upper limit of the reference range of 274 mu g.l(-1) in seven patients, with a maximal value of 1,881 mu g.l(-1) after multiple surfactant administrations. In contrast, 12 infants from Group II showed no increase in median E-alpha(1)-PI levels (Day 1 107 vs Day 2 107 mu g.l(-1)), and remained within the reference range (Day 1 125 mu g.l(-1); Day 2 107 mu g.l(-1)) of the 92 newborns without respiratory impairment, infection, birth-trauma or asphyxia.

From these results, it is concluded that surfactant may trigger a transient, mainly local, inflammatory response, reflected by increased levels of E-alpha(1)-PI, and may exert a dose-related pathogenic influence on the course and prognosis of RDS. Under these conditions, the validity of E-alpha(1)-PI for the diagnosis of early-onset septicaemia may be limited.

L23 ANSWER 4 OF 4 EMBASE

94314506 EMBASE Document No.: 1994314506. The Dutch hypothesis revisited: Recent evidence that children do not outgrow asthma. O'Brien K.P.; Fischer T.J.. Division of Allergy-Immunology, Children's Hospital Medical Center, Elland and Bethesda Ave,Cincinnati, OH 45229, United States. Pediatric Asthma, Allergy and Immunology Vol. 7, No. 2, pp. 89-97 1993.
ISSN: 0883-1874. CODEN: PAAIEP
Pub. Country: United States. Language: English. Summary Language: English.
Entered STN: 941102. Last Updated on STN: 941102

AB The phenotype termed 'asthma' now appears to represent a heterogeneous group of genetic defects, and as with any genetic condition, one should not be expected to outgrow the underlying pathology. Though anecdotal experience supports the impression that children outgrow asthma, perhaps they only outgrow their pediatrician. The current review presents the evidence that abnormalities in these children persist that should perhaps be followed. Anatomic considerations are discussed that can account for the disappearance of wheezing in early childhood despite continued presence of inflammation. Long-term follow-up studies confirm the persistence of abnormal bronchoscopy and spirometry findings. Six risk factors are presented that have been proposed to help identify those individuals at risk of excessive lung function decline in later adulthood. Successful prevention by inhaled corticosteroids is discussed. The evidence favors that (1) outgrowing asthma can be a misnomer, (2) there is a subset of postviral wheezers not persisting past age 10 years, but there is also a sizable cohort of postwheezing children who still have asthma that needs to be followed, (3) many COPD patients could actually represent end-stage mild asthma, (4) screening of adults who have outgrown asthma should be done more often, (5) education and counseling should be done so that the patient knows the importance of follow-up, and (6) high-risk

patients (identified by predictors of lung decline) might benefit from inhaled corticosteroids and yearly spirometry.

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=> s l19 and complex
L24        1747 L19 AND COMPLEX

=> s l24 and "C reactive protein"
L25          26 L24 AND "C REACTIVE PROTEIN"

=> s l25 and VLDL
L26          15 L25 AND VLDL

=> dup remove l26
PROCESSING COMPLETED FOR L26
L27            7 DUP REMOVE L26 (8 DUPLICATES REMOVED)

=> d l27 1-7 cbib abs

L27  ANSWER 1 OF 7     MEDLINE on STN                        DUPLICATE 1
2004093861.    PubMed ID: 14983228.   Prothrombinase enhancement through
     quantitative and qualitative changes affecting very low density
     lipoprotein in complex with C-reactive
     protein. Dennis Michael W; Downey Colin; Brufatto
     Nicole; Nesheim Michael E; Stevenson Ken; Toh Cheng Hock
     . (Roald Dahl Haemostasis & Thrombosis Centre, Royal Liverpool University
     Hospital, Prescot Street, Liverpool L7 8XP, United Kingdom. ) Thrombosis
     and haemostasis, (2004 Mar) Vol. 91, No. 3, pp. 522-30.  Journal code:
     7608063. ISSN: 0340-6245. Pub. country: Germany: Germany, Federal Republic
     of. Language: English.
AB   The biphasic waveform that can predict for disseminated intravascular
     coagulation (DIC) is due to the formation of a calcium-dependent
     complex between C reactive protein
     (CRP) and very low density lipoprotein (VLDL).  As thrombin
     generation is pivotal to DIC, this aspect has been specifically
     investigated and the VLDL component has been found to increase
     prothrombinase activity via both quantitative and qualitative changes.
     The specific prothrombinase activity of VLDL from patients
     manifesting the biphasic waveform was 2.5 times that of normal individuals
     or critically ill patients without the biphasic waveform.  This activity
     was due to an increase in anionic phospholipid surfaces that could be
     inhibited with excess annexin V and which was dependent on structurally
     intact apolipoprotein B.  The qualitative change appeared to be due to a
     deficiency of phosphatidylethanolamine in VLDL from patients
     with the biphasic waveform.  The functional consequence of this enhanced
     prothrombinase activity was an increased procoagulant effect in plasma.
     Using a modified activated partial thromboplastin time assay, the mean
     normal clot time decreased significantly when VLDL from patients
     with biphasic waveforms was substituted.  These results indicate that
     VLDL derived from patients with the biphasic waveform can enhance
     thrombin procoagulant activity.  As the CRP-VLDL complex
     exists in vivo, it could have a pathogenic role in disseminating the
     process of intravascular coagulation.

L27  ANSWER 2 OF 7  BIOSIS  COPYRIGHT (c) 2006 The Thomson Corporation  on STN
2004:167455  Document No.: PREV200400161711. Procoagulant enhancement through
     quantitative and qualitative changes affecting very low density
     lipoprotein in complex with C-reactive
     protein. Toh, Cheng Hock [Reprint Author]; Dennis,
     Michael W. [Reprint Author]; Colin, Downey [Reprint Author]. Roald Dahl
     Haemostasis and Thrombosis Unit, Royal Liverpool University Hospital,
     Liverpool, UK. Blood, (November 16 2003) Vol. 102, No. 11, pp. 90b. print.
     Meeting Info.: 45th Annual Meeting of the American Society of Hematology.
     San Diego, CA, USA. December 06-09, 2003. American Society of Hematology.
     CODEN: BLOOAW. ISSN: 0006-4971. Language: English.
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AB A complex between C reactive protein (CRP) and very low density lipoprotein (VLDL) is the molecular mechanism underlying the biphasic waveform that can predict for disseminated intravascular coagulation (DIG). To ascertain if it plays a role in the disease process rather than just as a predictive marker, we have established that there is a virtual 100% correlation to clinical DIC at maximal levels of complex formation in patient plasma. It also exists in vivo as demonstrated by size-exclusion chromatography and the quantitation of CRP within isolated VLDL fractions. We have now found that VLDL from patients with the biphasic waveform only supports increased prothrombinase activity via both quantitative VLDL triglyceride increases (up to 4 mM triglyceride) and qualitative changes with 2.5 times the specific prothrombinase activity of VLDL from normal or critically ill individuals without the biphasic waveform. This activity can be inhibited with excess annexin V at 5 mM CaCl2 and depends on intact apolipoprotein (apo) B but not apo E. Flow cytometric analysis after apo B immunoadsorption shows no intact VLDL particles suggesting that the role of apo B is as structural support for the requisite phospholipid conformation. Further qualitative assessment of the VLDL by 2 dimensional thin layer chromatography demonstrated an absence of phosphatidylethanolamine in VLDL from patients with the biphasic waveform only. To ascertain if these changes responsible for increasing thombin generation had functional consequences on coagulation in plasma, a modified activated partial thromboplastin time assay was used. The addition into normal plasma of isolated VLDL from patients with the biphasic waveform significantly shortened clot time. The mean clot time was 203 seconds (SEM 0.95) for VLDL from 7 normal unrelated donors and this decreased to 178 seconds (SEM 3.02) for VLDL from 7 patients with biphasic waveforms. There is dose-dependence of this effect as increasing proportional ratios of VLDL from patients admixed to normal VLDL shortened the clot time proportionately in all 6 cases with a plateauing of effect in 2 experiments. Taken together, these results indicate that the CRP-VLDL complex can enhance the pro-coagulant aspects of thrombin generation. It could therefore have a pathogenic role in disseminating the process of intravascular coagulation.

L27 ANSWER 3 OF 7 MEDLINE on STN DUPLICATE 2

2002496203. PubMed ID: 12239165. Biphasic transmittance waveform in the APTT coagulation assay is due to the formation of a Ca(++)-dependent complex of C-reactive protein with very-low-density lipoprotein and is a novel marker of impending disseminated intravascular coagulation. Toh Cheng Hock; Samis John; Downey Colin; Walker John; Becker Lev; Brufatto Nicole; Tejidor Liliana; Jones Greg; Houdijk Wim; Giles Alan; Koschinsky Marlys; Ticknor Larry O; Paton Ray; Wenstone Richard; Nesheim Michael. (Departments of Biochemistry and Pathology, Queen's University, Kingston, ON, Canada.) Blood, (2002 Oct 1) Vol. 100, No. 7, pp. 2522-9. Journal code: 7603509. ISSN: 0006-4971. Pub. country: United States. Language: English.

AB A decrease in light transmittance before clot formation, manifesting as a biphasic waveform (BPW) pattern in coagulation assays, was previously correlated with the onset of disseminated intravascular coagulation (DIC). In this study of 1187 consecutive admissions to the intensive care unit, the degree of this change on admission predicts DIC better than D-dimer measurements. Additionally, the BPW preceded the time of DIC diagnosis by 18 hours, on average, in 56% (203 of 362) of DIC patients. The BPW is due to the rapid formation of a precipitate and coincident turbidity change on recalcification of plasma. The isolated precipitate contains very-low-density lipoprotein (VLDL) and C-reactive protein (CRP). The addition of CRP and Ca(++) to normal plasma also causes the precipitation of VLDL and IDL, but not LDL or HDL. The K(d) of the CRP/VLDL interaction is 340 nM, and the IC(50) for Ca(++) is 5.0 mM. In 15 plasmas with the BPW, CRP

was highly elevated (77-398 microg/mL), and the concentration of isolated VLDL ranged from 0.082 to 1.32 mM (cholesterol). The turbidity change on recalcification correlates well with the calculated level of the CRP-VLDL complex. Clinically, the BPW better predicts for DIC than either CRP or triglyceride alone. The complex may have pathophysiological implications because CRP can be detected in the VLDL fraction from sera of patients with the BPW, and the VLDL fraction has enhanced prothrombinase surface activity. The complex has been designated lipoprotein complexed C-reactive protein.

L27 ANSWER 4 OF 7 MEDLINE on STN

2002692293. PubMed ID: 12452811. Waveform analysis of clotting test optical profiles in the diagnosis and management of disseminated intravascular coagulation (DIC). Toh C H; Giles A R. (Roald Dahl Haemostasis and Thrombosis Centre, Royal Liverpool University Hospital, Liverpool, UK.. toh@liverpool.ac.uk) . Clinical and laboratory haematology, (2002 Dec) Vol. 24, No. 6, pp. 321-7. Ref: 15. Journal code: 7907061. ISSN: 0141-9854. Pub. country: England: United Kingdom. Language: English.

AB Transmittance waveform charts the changes in light transmittance on standard coagulation assays, such as the prothrombin time (PT) and activated partial thromboplastin time (APTT). Analysis and characterization of these data on photo-optical coagulation analysers provides additional qualitative and quantitative information to that obtained using the clotting time alone. The most thoroughly evaluated clinical application is that of the biphasic APTT waveform with disseminated intravascular coagulation (DIC). The degree of waveform abnormality correlates directly with the severity of haemostatic dysfunction and allows for both the prediction and monitoring from non-overt to overt DIC. As its performance is simple and rapid, this provides the means for targeting therapeutic intervention to an earlier stage of DIC. The recent identification that the mechanism underlying the biphasic waveform is a complex that exists in vivo between C reactive protein with very low density lipoprotein, provides potentially important insights into the molecular pathogenesis of DIC. Thus, in addition to the immediate clinical utility in diagnostic practice, it has important applications as a research tool. Preliminary experience in the application of this technology to the diagnosis and management of the haemophilias and the lupus anticoagulant syndrome has also provided evidence of the power and utility of waveform analysis in essentially simple clotting assays.

L27 ANSWER 5 OF 7 MEDLINE on STN

2003382682. PubMed ID: 12918783. Lipoprotein-complexed C-reactive protein and the biphasic transmittance waveform in critically ill patients. Nesheim Michael; Samis John ; Walker John; Becker Lev; Brufatto Nicole; Fischer Timothy; Tejidor Liliana; Jones Greg; Houdijk Wim; Giles Alan; Koschinsky Marlys; Wenstone Richard; Downey Colin; Toh Cheng Hock. (Department of Biochemistry, Queen's University, Kingston, Ontario, Canada.. nesheimm@post.queensu.ca) . Blood reviews, (2002 Dec) Vol. 16 Suppl 1, pp. S15-22. Journal code: 8708558. ISSN: 0268-960X. Pub. country: Scotland: United Kingdom. Language: English.

AB The 'biphasic transmittance waveform' (BTW) refers to a decrease in light transmittance that often occurs prior to clotting in coagulation assays of critically ill patient plasmas. It correlates with disseminated intravascular coagulation and mortality. The present work shows that the BTW is due to the rapid formation of a precipitate and a coincident change in turbidity in re-calcified plasma. The precipitate was isolated from patient plasma and contained lipids typical of very low density lipoprotein (VLDL), plus the proteins apolipoprotein B-100 and C-reactive protein (CRP). Precipitation also occurred in normal plasma supplemented with CRP. In addition, CRP precipitated with VLDL and intermediate density lipoprotein, but

not low density lipoprotein or high density lipoprotein. The Kd value for the CRP/VLDL interaction is 340 nM. The IC50 value of Ca2+ for complex formation is 5.0 mM, and epsilon-aminocaproic acid inhibits the process. In 15 plasmas with the BTW from critically ill patients, CRP was highly elevated (77-398 microg/mL) and VLDL cholesterol ranged from 0.082 to 1.32 mM. The magnitude of the turbidity change on re-calcification correlated well with the calculated level of the CRP/VLDL complex. Thus, the Ca2+-dependent formation of a complex between CRP and VLDL accounts for the BTW.

L27 ANSWER 6 OF 7 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN
2001:301143 Document No.: PREV200100301143. In vitro binding of C-reactive protein to very low and intermediate density . lipoproteins in a calcium-dependent complex. Perez, U. [Reprint author]; Hoke, R. [Reprint author]; Doobay, H. [Reprint author]; Fischer, T. [Reprint author]; Samis, J.; Nesheim, M.; Tejidor, L. [Reprint author]. Hemostasis Reagent Development, Organon Teknika Corporation, Durham, NC, USA. Blood, (November 16, 2000) Vol. 96, No. 11 Part 2, pp. 76b. print.
Meeting Info.: 42nd Annual Meeting of the American Society of Hematology. San Francisco, California, USA. December 01-05, 2000. American Society of Hematology.
CODEN: BLOOAW. ISSN: 0006-4971. Language: English.

AB The presence of a biphasic aPTT waveform has been correlated to negative outcome for patients in the intensive care setting (Downey C, et al. Early Identification and Prognostic Implications in Disseminated Intravascular Coagulation through Transmittance Waveform Analysis. Thromb Haemost 1998; 80: 65-9). It has recently been discovered that the mechanism underlying the atypical biphasic aPTT waveform is the result of the formation of a complex between C-reactive protein (CRP) with very low and intermediate density lipoprotein (VLDL or IDL) in a divalent cation-dependent reaction. The complex has been termed LC-CRP for "Lipoprotein-Complexed C-Reactive Protein". Initially, it was demonstrated that CRP isolated from patient plasma formed the complex when added to normal plasma. A possible mechanism for complex formation could be the result of qualitative differences in either CRP or the lipoproteins. To address this, recombinant CRP (rCRP) was combined in vitro with various lipoprotein subfractions. Free and bound CRP were quantified by ELISA. Results showed that rCRP was indistinguishable from patient CRP and that complex formation was specific for the VLDL/IDL subfraction. Recombinant CRP did not form a complex with LDL or HDL. Binding was inhibited by 1 mM phosphorylcholine, suggesting the involvement of the phosphatidylcholine lipid headgroups during complex formation. While these results may suggest that qualitative differences in CRP do not account for LC-CRP formation, they also enable the development of a quantitative assay for LC-CRP. An LC-CRP calibrator was constructed by mixing VLDL (0.24 mg/mL cholesterol) and CRP (200 mug/mL) in lipoprotein deficient plasma. By measuring the initial absorbance rate, dilutions in a plasma base provided a linear dose-response curve. As a synthetic VLDL substitute, artificial vesicles prepared from mixtures of phosphatidylcholine and lysophosphatidylcholine bound moderately to CRP. Development of a quantitative assay for LC-CRP that is fully automated and adaptable to multiple instrument platforms would allow direct measurement of the complex and has the potential to aid in therapeutic intervention and monitoring in this critically ill patient population.

L27 ANSWER 7 OF 7 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN
2001:311730 Document No.: PREV200100311730. The biphasic waveform in the MDA system coagulation analyzer is due to the Ca++-induced formation and precipitation of a complex of very low density lipoprotein and C-reactive protein. Nesheim, Michael

E. [Reprint author]; Samis, John [Reprint author]; Walker, John [Reprint author]; Fischer, Tim; Tejidor, Liliana; Houdijk, Wim; Giles, Alan; Becker, Lev [Reprint author]; Koschinsky, Marlys [Reprint author]; Downey, Colin; Toh, Cheng Hock. Biochemistry, Queen's University, Kingston, ON, Canada. Blood, (November 16, 2000) Vol. 96, No. 11 Part 1, pp. 50a-51a. print.
Meeting Info.: 42nd Annual Meeting of the American Society of Hematology. San Francisco, California, USA. December 01-05, 2000. American Society of Hematology.
CODEN: BLOOAW. ISSN: 0006-4971. Language: English.

AB Downey, et al. recently showed that decreased light transmission prior to clot formation in the APPT assay using the Organon Teknika MDA-180 correlated with negative outcome for patients in intensive care (Thromb. and Haemost. 80, 65-9, 1998). The phenomenon was designated the "biphasic waveform" (BWF). In order to identify and characterize the molecular basis for the BWF, an assay based on the turbidity increase which occurs when mixtures of normal and patient plasmas are recalcified in the presence of a thrombin inhibitor was devised. The increase in turbidity was due to precipitate formation in positive samples. The precipitate was isolated from a pool of eight patient plasmas. Lipid and protein analysis showed that the precipitate contained components typical of very low density lipoprotein (VLDL) and C-reactive protein (CRP). Fractionation of the redissolved precipitate by ion exchange resolved the VLDL components from the CRP, neither of which alone would form a precipitate when recalcified, although a mixture of them would. Normal plasma supplemented with CRP formed a precipitate when recalcified. Further work showed that CRP readily forms a Ca++-dependent precipitate with purified VLDL and intermediate density lipoprotein (IDL), but not with low or high density lipoproteins. The interaction between normal VLDL and recombinant CRP exhibits a dissociation constant of 340nM (expressed relative to the CRP concentration) and VLDL at 1mM cholesterol binds 178mug CRP/ml. Binding is half maximal at 5.0mM Ca++. Fifteen patient plasmas with a BWF were analyzed with respect to the magnitude of the turbidity change upon reclacification and the concentrations of VLDL and CRP. The VLDL cholesterol levels ranged from 0.095 to 1.32mM, and the CRP levels were 77 to 398 mug/ml. The turbidity change correlated linearly with the VLDL level, but not with the level of CRP, which was always in excess. We conclude that the BWF is due to formation of a very high molecular weight, Ca++-dependent complex between C -reactive protein, VLDL and possibly IDL.

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=> s l25 and IDL
L28           7 L25 AND IDL

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PROCESSING COMPLETED FOR L28
L29           3 DUP REMOVE L28 (4 DUPLICATES REMOVED)

=> d l29 1-3 cbib abs

L29  ANSWER 1 OF 3     MEDLINE on STN                    DUPLICATE 1
2002496203.    PubMed ID: 12239165.   Biphasic transmittance waveform in the
     APTT coagulation assay is due to the formation of a Ca(++)-dependent
     complex of C-reactive protein with
     very-low-density lipoprotein and is a novel marker of impending
     disseminated intravascular coagulation. Toh Cheng Hock;
     Samis John; Downey Colin; Walker John; Becker
     Lev; Brufatto Nicole; Tejidor Liliana; Jones Greg; Houdijk Wim;
     Giles Alan; Koschinsky Marlys; Ticknor Larry O; Paton Ray; Wenstone
     Richard; Nesheim Michael. (Departments of Biochemistry and
     Pathology, Queen's University, Kingston, ON, Canada. ) Blood, (2002 Oct 1)
     Vol. 100, No. 7, pp. 2522-9.  Journal code: 7603509. ISSN: 0006-4971. Pub.
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country: United States. Language: English.

AB A decrease in light transmittance before clot formation, manifesting as a biphasic waveform (BPW) pattern in coagulation assays, was previously correlated with the onset of disseminated intravascular coagulation (DIC). In this study of 1187 consecutive admissions to the intensive care unit, the degree of this change on admission predicts DIC better than D-dimer measurements. Additionally, the BPW preceded the time of DIC diagnosis by 18 hours, on average, in 56% (203 of 362) of DIC patients. The BPW is due to the rapid formation of a precipitate and coincident turbidity change on recalcification of plasma. The isolated precipitate contains very-low-density lipoprotein (VLDL) and C-reactive protein (CRP). The addition of CRP and Ca(++) to normal plasma also causes the precipitation of VLDL and IDL, but not LDL or HDL. The K(d) of the CRP/VLDL interaction is 340 nM, and the IC(50) for Ca(++) is 5.0 mM. In 15 plasmas with the BPW, CRP was highly elevated (77-398 microg/mL), and the concentration of isolated VLDL ranged from 0.082 to 1.32 mM (cholesterol). The turbidity change on recalcification correlates well with the calculated level of the CRP-VLDL complex . Clinically, the BPW better predicts for DIC than either CRP or triglyceride alone. The complex may have pathophysiological implications because CRP can be detected in the VLDL fraction from sera of patients with the BPW, and the VLDL fraction has enhanced prothrombinase surface activity. The complex has been designated lipoprotein complexed C-reactive protein.

L29 ANSWER 2 OF 3 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN

2001:301143 Document No.: PREV200100301143. In vitro binding of C-reactive protein to very low and intermediate density lipoproteins in a calcium-dependent complex. Perez, U. [Reprint author]; Hoke, R. [Reprint author]; Doobay, H. [Reprint author]; Fischer, T. [Reprint author]; Samis, J.; Nesheim, M.; Tejidor, L. [Reprint author]. Hemostasis Reagent Development, Organon Teknika Corporation, Durham, NC, USA. Blood, (November 16, 2000) Vol. 96, No. 11 Part 2, pp. 76b. print.
Meeting Info.: 42nd Annual Meeting of the American Society of Hematology. San Francisco, California, USA. December 01-05, 2000. American Society of Hematology.
CODEN: BLOOAW. ISSN: 0006-4971. Language: English.

AB The presence of a biphasic aPTT waveform has been correlated to negative outcome for patients in the intensive care setting (Downey C, et al. Early Identification and Prognostic Implications in Disseminated Intravascular Coagulation through Transmittance Waveform Analysis. Thromb Haemost 1998; 80: 65-9). It has recently been discovered that the mechanism underlying the atypical biphasic aPTT waveform is the result of the formation of a complex between C-reactive protein (CRP) with very low and intermediate density lipoprotein (VLDL or IDL) in a divalent cation-dependent reaction. The complex has been termed LC-CRP for "Lipoprotein-Complexed C-Reactive Protein". Initially, it was demonstrated that CRP isolated from patient plasma formed the complex when added to normal plasma. A possible mechanism for complex formation could be the result of qualitative differences in either CRP or the lipoproteins. To address this, recombinant CRP (rCRP) was combined in vitro with various lipoprotein subfractions. Free and bound CRP were quantified by ELISA. Results showed that rCRP was indistinguishable from patient CRP and that complex formation was specific for the VLDL/IDL subfraction. Recombinant CRP did not form a complex with LDL or HDL. Binding was inhibited by 1 mM phosphorylcholine, suggesting the involvement of the phosphatidylcholine lipid headgroups during complex formation. While these results may suggest that qualitative differences in CRP do not account for LC-CRP formation, they also enable the development of a quantitative assay for LC-CRP. An LC-CRP calibrator was constructed by mixing VLDL (0.24 mg/mL cholesterol) and CRP (200 mug/mL) in lipoprotein deficient plasma. By measuring the initial absorbance rate, dilutions in

a plasma base provided a linear dose-response curve. As a synthetic VLDL substitute, artificial vesicles prepared from mixtures of phosphatidylcholine and lysophosphatidylcholine bound moderately to CRP. Development of a quantitative assay for LC-CRP that is fully automated and adaptable to multiple instrument platforms would allow direct measurement of the complex and has the potential to aid in therapeutic intervention and monitoring in this critically ill patient population.

L29 ANSWER 3 OF 3 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN
2001:311730 Document No.: PREV200100311730. The biphasic waveform in the MDA system coagulation analyzer is due to the Ca++-induced formation and precipitation of a complex of very low density lipoprotein and C-reactive protein. Nesheim, Michael E. [Reprint author]; Samis, John [Reprint author]; Walker, John [Reprint author]; Fischer, Tim; Tejidor, Liliana; Houdijk, Wim; Giles, Alan; Becker, Lev [Reprint author]; Koschinsky, Marlys [Reprint author]; Downey, Colin; Toh, Cheng Hock. Biochemistry, Queen's University, Kingston, ON, Canada. Blood, (November 16, 2000) Vol. 96, No. 11 Part 1, pp. 50a-51a. print.
Meeting Info.: 42nd Annual Meeting of the American Society of Hematology. San Francisco, California, USA. December 01-05, 2000. American Society of Hematology.
CODEN: BLOOAW. ISSN: 0006-4971. Language: English.
AB Downey, et al. recently showed that decreased light transmission prior to clot formation in the APPT assay using the Organon Teknika MDA-180 correlated with negative outcome for patients in intensive care (Thromb. and Haemost. 80, 65-9, 1998). The phenomenon was designated the "biphasic waveform" (BWF). In order to identify and characterize the molecular basis for the BWF, an assay based on the turbidity increase which occurs when mixtures of normal and patient plasmas are recalcified in the presence of a thrombin inhibitor was devised. The increase in turbidity was due to precipitate formation in positive samples. The precipitate was isolated from a pool of eight patient plasmas. Lipid and protein analysis showed that the precipitate contained components typical of very low density lipoprotein (VLDL) and C-reactive protein (CRP). Fractionation of the redissolved precipitate by ion exchange resolved the VLDL components from the CRP, neither of which alone would form a precipitate when recalcified, although a mixture of them would. Normal plasma supplemented with CRP formed a precipitate when recalcified. Further work showed that CRP readily forms a Ca++-dependent precipitate with purified VLDL and intermediate density lipoprotein (IDL), but not with low or high density lipoproteins. The interaction between normal VLDL and recombinant CRP exhibits a dissociation constant of 340nM (expressed relative to the CRP concentration) and VLDL at 1mM cholesterol binds 178mug CRP/ml. Binding is half maximal at 5.0mM Ca++. Fifteen patient plasmas with a BWF were analyzed with respect to the magnitude of the turbidity change upon reclacification and the concentrations of VLDL and CRP. The VLDL cholesterol levels ranged from 0.095 to 1.32mM, and the CRP levels were 77 to 398 mug/ml. The turbidity change correlated linearly with the VLDL level, but not with the level of CRP, which was always in excess. We conclude that the BWF is due to formation of a very high molecular weight, Ca++-dependent complex between C-reactive protein, VLDL and possibly IDL.

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=> s l24 and "serum amyloid A"
L30             1 L24 AND "SERUM AMYLOID A"

=> d l30 cbib abs

L30  ANSWER 1 OF 1  CAPLUS  COPYRIGHT 2006 ACS on STN
2002:966970   Document No. 138:21824  Method for detecting a lipoprotein-acute
     phase protein complex and predicting an increased risk of system
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failure or mortality. Fischer, Timothy J.; Downey, Colin; Nesheim, Mike; Samis, John A.; Tejidor, Liliana; Toh, Cheng Hock; Walker, John B. (USA). U.S. Pat. Appl. Publ. US 2002193949 A1 20021219, 47 pp., Cont.-in-part of U. S. Ser. No. 591,642, abandoned. (English). CODEN: USXXCO. APPLICATION: US 2001-19087 20011219. PRIORITY: US 1995-477839 19950607; US 1997-859773 19970521; US 1997-1647 19971231; US 1999-244340 19990204; US 2000-591642 20000609; WO 2001-US18611 20010608.

AB A method for diagnosing a condition of a patient involves the steps of (a) adding one or more reagents to a test sample from a patient, the test samples comprising at least part of a blood sample from the patient, in order to cause formation of a complex comprising at least one acute phase protein at least one human lipoprotein, while causing substantially no fiber polymerization; (b) measuring the formation of the complex over time so as to derive a time-dependent measurement profile, and (c) determining a slope and/or total change in the time-dependent measurement profile, so as to diagnose a condition of the patient. A greater formation of the complex is correlated to increased probability of death of the patient.

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---Logging off of STN---

=>
Executing the logoff script...

=> LOG Y

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	210.12	210.33

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	-9.75	-9.75

STN INTERNATIONAL LOGOFF AT 10:12:05 ON 06 JUL 2006